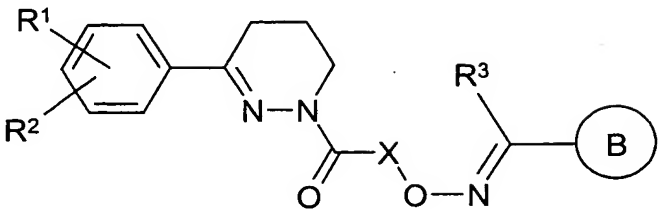
Patent Claims

1. Compounds of the formula I



I

in which

R^1, R^2 are each, independently of one another, H, OH, OR^8, $-SR^8$, $-SOR^8$, $-SO_2R^8$ or Hal,

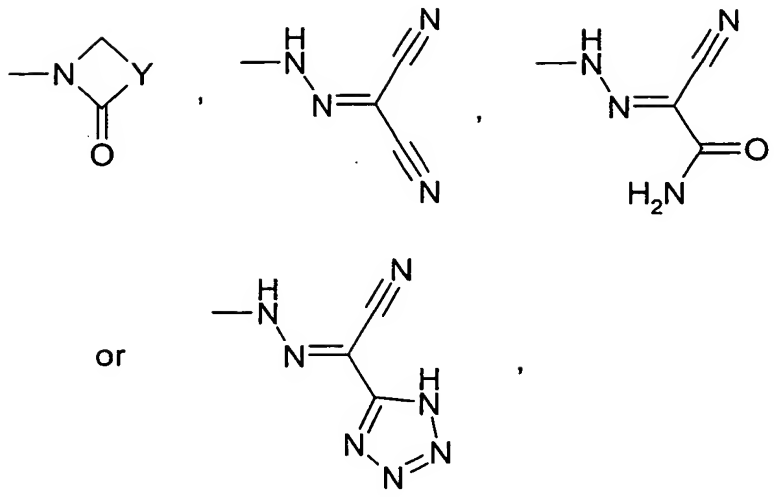
R^1 and R^2 together are alternatively $-OCH_2O-$ or $-OCH_2CH_2O-$,

R^3 is H, $A"R^7$, $COA"R^7$, $COOA"R^7$, $CONH_2$, $CONHA"R^7$, $CON(A"R^7)(A'"R^7)$, $CONR^{10}Het$, NH_2, $NHA"R^7$, $N(A"R^7)(A'"R^7)$, $NCOA"R^7$ or $NCOOA"R^7$,

B is an aromatic isocyclic or heterocyclic radical, which may be unsubstituted or monosubstituted, disubstituted or trisubstituted by R^4, R^5 and/or R^6,

X is alkylene having 1-10 carbon atoms or alkenylene having 2-8 carbon atoms,
in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH or $NA"R^7$,
1-7 H atoms may be replaced by F and/or Cl,

R^4, R^5, R^6 are each, independently of one another, H, $A"R^7$, OH, $OA"R^7$, NO_2, NH_2, $NHA"R^7$, $N(A"R^7)(A'"R^7)$, $NHCOA"R^7$, $NHCOOA"R^7$, $NHCONH_2$, $NHCONHA"R^7$, $NHCON(A"R^7)(A'"R^7)$, Hal, COOH, $COOA"R^7$, $CONH_2$, $CONHA"R^7$, $CON(A"R^7)(A'"R^7)$,



	R^7	is H, COOH, COOA, $CONH_2$, CONHA, CONAA', NH_2, NHA, NAA', NCOA, NCOOA, OH or OA,
5	R^8	is A, cycloalkyl having 3-7 carbon atoms, alkylenecycloalkyl having 4-8 carbon atoms or alkenyl having 2-8 carbon atoms,
	R^9	is alkyl having 1-10 carbon atoms, cycloalkyl having 3-7 carbon atoms, alkylenecycloalkyl having 4-8 carbon atoms
10		or alkenyl having 2-8 carbon atoms, in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH, NMe, NEt and/or by –CH=CH- groups, 1-7 H atoms may be replaced by F and/or Cl, and/or 1 H atom may be replaced by R^7,
15	Y	is alkylene having 1-10 carbon atoms or alkenylene having 2-8 carbon atoms, in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH or NR^9 and/or 1-7 H atoms may be replaced by F and/or Cl,
20	A, A'	are each, independently of one another, alkyl having 1-10 carbon atoms or alkenyl having 2-8 carbon atoms, in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH or NR^9 and/or 1-7 H atoms may be replaced by F and/or Cl,

or
aryl or Het,

A and A' together are alternatively an alkylene chain having 2-7 carbon atoms, in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH, NR^9, $NCOR^9$ or $NCOOR^9$,

A'', A''' are each, independently of one another,
absent, alkylene having 1-10 carbon atoms, alkenylene having 2-8 carbon atoms or cycloalkylene having 3-7 carbon atoms,
in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH or NR^9 and/or
1-7 H atoms may be replaced by F and/or Cl,

A'' and A''' together are alternatively an alkylene chain having 2-7 carbon atoms, in which one, two or three CH_2 groups may be replaced by O, S, SO, SO_2, NH, NR^9, $NCOR^9$ or $NCOOR^9$,

aryl is phenyl, naphthyl, fluorenyl or biphenyl, each of which is unsubstituted or monosubstituted, disubstituted or trisubstituted by Hal, R^{11}, OR^{10}, $N(R^{10})_2$, NO_2, CN, $COOR^{10}$, $CON(R^{10})_2$, $NR^{10}COR^{10}$, $NR^{10}CON(R^{10})_2$, $NR^{10}SO_2A$, COR^{10}, $SO_2N(R^{10})_2$, $S(O)_mR^{11}$,

R^{10} is H or alkyl having 1-6 carbon atoms,

R^{11} is alkyl having 1-6 carbon atoms,

Het is a monocyclic or bicyclic saturated, unsaturated or aromatic heterocyclic ring having 1 to 2 N, O and/or S atoms, which may be unsubstituted or monosubstituted or disubstituted by carbonyl oxygen, Hal, R^{11}, OR^{10}, $N(R^{10})_2$, NO_2, CN, $COOR^{10}$, $CON(R^{10})_2$, $NR^{10}COR^{10}$, $NR^{10}CON(R^{10})_2$, $NR^{10}SO_2R^{11}$, COR^{10}, SO_2NR^{10} and/or $S(O)_mR^{11}$,

Hal is F, Cl, Br or I,

m is 0, 1 or 2,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1, in which

R^1, R^2 are each, independently of one another, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1, in which

R^1, R^2 are each, independently of one another, H, methoxy, ethoxy, benzyloxy, propoxy, isopropoxy, difluoromethoxy, F, Cl, cyclopentyloxy, cyclohexyloxy or cycloheptyloxy,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

4. Compounds according to Claim 1, in which

R^1, R^2 are each, independently of one another, methoxy, ethoxy, propoxy, isopropoxy, cyclopentyloxy or F,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4, in which

R^1 is 4-methoxy,

R^2 is 3-ethoxy or 3-propoxy,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5, in which

R^3 is H, A"R^7, COA"R^7, CON(A"R^7)(A'"R^7) or CO-NR^{10}-Het,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-6,

in which

X is methylene, ethylene, propylene or butylene,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7,

in which

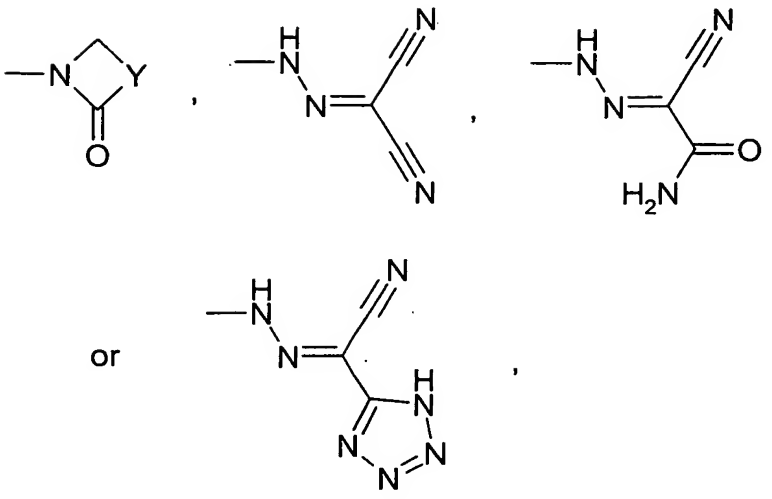
B is phenyl, pyridyl, pyridyl N-oxide, thienyl, furyl, pyrrolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, isoxazolinyl, oxazolinyl, thiazolinyl, pyrazolinyl, imidazolinyl, naphthyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl or quinoxalinyl, each of which is unsubstituted or may be monosubstituted, disubstituted or trisubstituted by R^4, R^5 and/or R^6,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8,

in which

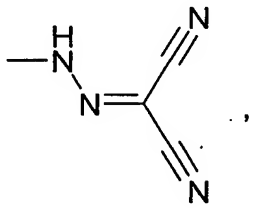
B is phenyl, pyridyl, pyridyl N-oxide, thienyl, furyl, pyrrolyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, isoxazolinyl, oxazolinyl, thiazolinyl, pyrazolinyl, imidazolinyl, naphthyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl or quinoxalinyl, each of which is unsubstituted or may be monosubstituted, disubstituted or trisubstituted by OH, OA, NO_2, NH_2, NAA',



and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

B is phenyl which is unsubstituted or monosubstituted by OR^{10}, NO_2 or



or unsubstituted pyridyl or pyridyl N-oxide,
and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

11. Compounds according to one or more of Claims 1-10, in which

R^1, R^2 are each, independently of one another, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms,

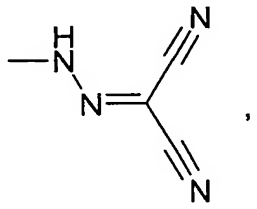
X is methylene, ethylene, propylene or butylene,

R^3 is H, A"R^7, COA"R^7, CON(A"R^7)(A'"R^7) or CO-NR^{10}-Het,

A", A'" are each, independently of one another, absent or alkylene having 1-10 carbon atoms, in which one CH_2 group may be replaced by NH or NR^9,

A", A'" together are alternatively an alkylene chain having 2-7 carbon atoms, in which one CH_2 group may be replaced by NH or NR^9,

B is phenyl which is unsubstituted or monosubstituted by OR^{10}, NO_2,



, NH_2 or $NHCOOA"R^7$, or unsubstituted pyridyl or pyridyl N-oxide,

R^7 is H, COOH, NHA or NAA',

R^9 is alkyl having 1-6 carbon atoms,

R^{10} is H or alkyl having 1-6 carbon atoms,

A, A' are each, independently of one another, alkyl having 1-10 carbon atoms, in which 1-7 H atoms may be replaced by F and/or Cl,

Het is a monocyclic saturated heterocyclic radical having 1 to 2 N atoms, which may be monosubstituted or disubstituted by alkyl having 1-6 carbon atoms,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

12. Compounds according to one or more of Claims 1-11,

in which

R^1, R^2 are each, independently of one another, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms,

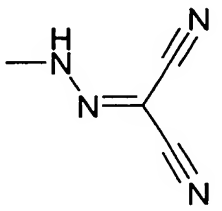
X is methylene, ethylene, propylene or butylene,

R^3 is H, $A"R^7$, $COA"R^7$, $CON(A"R^7)(A'"R^7)$ or $CO\text{-}NR^{10}$-Het,

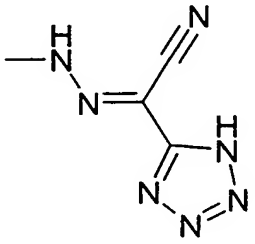
A", A'" are each, independently of one another, absent or alkylene having 1-10 carbon atoms, in which one CH_2 group may be replaced by NH or NR^9,

A", A'" together are alternatively an alkylene chain having 2-7 carbon atoms, in which one CH_2 group may be replaced by NH or NR^9,

B is phenyl which is unsubstituted or monosubstituted by OR^{10}, NO_2,



or



,

NH_2 or $NHCOOA"R^7$, or unsubstituted pyridyl or pyridyl N-oxide,

R^7 is H, COOH, NHA or NAA',

R^9 is alkyl having 1-6 carbon atoms,

R^{10} is H or alkyl having 1-6 carbon atoms,

A, A' are each, independently of one another, alkyl having 1-10 carbon atoms, in which 1-7 H atoms may be replaced by F and/or Cl,

Het is a monocyclic saturated heterocyclic radical having 1 to 2 N atoms, which may be monosubstituted or disubstituted by alkyl having 1-6 carbon atoms,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

13. Compounds of the formula I according to Claim 1 from the group consisting of

a) 4-methoxybenzaldehyde O-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

b) benzaldehyde O-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

c) 4-hydroxybenzaldehyde O-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

d) pyridine-4-carbaldehyde O-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

e) 1-oxypyridine-4-carbaldehyde O-{2-[3-(3-ethoxy-4-methoxy-phenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

f) 4-methoxybenzaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

g) benzaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

h) pyridine-4-carbaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

i) 1-oxypyridine-4-carbaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

j) 4-nitrobenzaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

k) 4-aminobenzaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

l) 4-tert-butyloxycarbonylaminobenzaldehyde O-{2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

m) 2-{[4-({2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}methyl)phenyl]hydrazono}malononitrile,

n) 2-{[3-({2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}methyl)phenyl]hydrazono}malononitrile,

o) 2-{[4-({2-[3-(4-methoxy-3-propoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}methyl)phenyl]hydrazono}-malononitrile,

p) {2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}-2-phenylacetic acid,

q) 2-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}-N-methyl-N-(1-methylpiperidin-4-yl)-2-phenylacetamide,

r) 1-(4-methylpiperazin-1-yl)-2-phenylethane-1,2-dione 2-(O-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethyl} oxime,

s) N-(2-dimethylaminoethyl)-2-{2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]-2-oxoethoxyimino}-2-phenylacetamide,

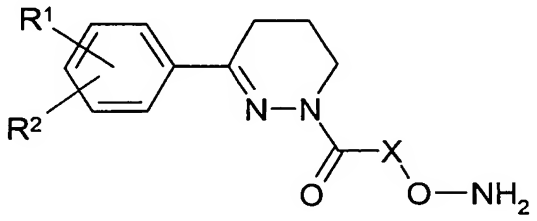
t) 2-{[4-({2-[3-(3-ethoxy-4-methoxyphenyl)-5,6-dihydro-4*H*-pyridazin-1-yl]-2-oxoethoxyimino}methyl)phenyl]hydrazono}-2-(1*H*-tetrazol-5-yl)acetonitrile,

and pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios.

14. Compounds of the formula I according to one or more of Claims 1 to 13 as phosphodiesterase IV inhibitors.

15. Process for the preparation of compounds of the formula I and salts and solvates thereof, characterised in that

a) a compound of the formula II

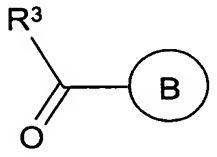


II

in which

X, R^1 and R^2 are as defined in Claim 1,

is reacted with a compound of the formula III



III

in which

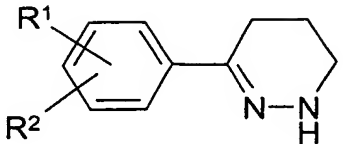
R^3 and B are as defined in Claim 1,

with the proviso that any further OH and/or amino group present is protected,

and subsequently, if desired, a protecting group is removed,

or

b) a compound of the formula IV

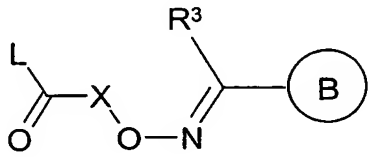


IV

in which

R^1 and R^2 are as defined in Claim 1,

is reacted with a compound of the formula V



V

in which

L is Cl, Br, I or a free or reactively functionally modified OH group,

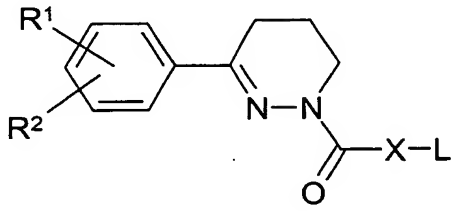
and R^3, X and B are as defined in Claim 1,

with the proviso that any further OH and/or amino group present is protected,

and subsequently, if desired, a protecting group is removed,

or

c) a compound of the formula VI



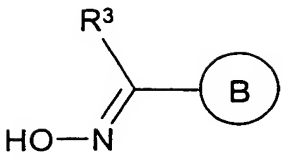
VI

in which

X, R^1 and R^2 are as defined in Claim 1, and

L is Cl, Br, I or a free or reactively functionally modified OH group,

is reacted with a compound of the formula VII



VII

in which R^3 and B are as defined in Claim 1,
with the proviso that any further OH and/or amino group present is protected,
and subsequently, if desired, a protecting group is removed,

or

d) one or more radicals R^1, R^2, R^3 and/or B in a compound of the formula I are converted into one or more other radicals R^1, R^2, R^3 and/or B by

i) cleaving an ether or ester,
ii) alkylating or acylating an OH function,
iii) reductively alkylating an amino group,
iv) reacting an amino group with malononitrile,
v) converting a cyano group into a tetrazole group,

and/or in that a basic compound of the formula I is converted into one of its salts by treatment with an acid.

16. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 13 and/or pharmaceutically usable derivatives, solvates, stereoisomers and E/Z isomers thereof, including mixtures thereof in all ratios, and, if desired, excipients and/or adjuvants.

17. Use of compounds of the formula I according to one or more of Claims 1 to 13 and/or physiologically acceptable salts or solvates thereof for the preparation of a medicament for the treatment of a patient

suffering from a disease or condition mediated by the PDE IV isozyme in its role in regulating the activation and degranulation of human eosinophils.

18. Use according to Claim 17 of compounds of the formula I according to one or more of Claims 1 to 13 and/or physiologically acceptable salts or solvates thereof for the preparation of a medicament for combating allergic diseases, asthma, chronic bronchitis, atopic dermatitis, psoriasis and other skin diseases, inflammatory diseases, autoimmune diseases, such as, for example, rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes mellitus or ulcerative colitis, osteoporosis, transplant rejection reactions, cachexia, tumour growth or tumour metastases, sepsis, memory disorders, atherosclerosis and AIDS.

19. Use according to Claim 17 or 18 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment or prevention of one or more of the diseases, pathological disorders and conditions from the following group:

asthma of whatever type, etiology or pathogenesis, or asthma selected from the group consisting of atopic asthma, non-atopic asthma, allergic asthma, atopic, IgE-mediated asthma, bronchial asthma, essential asthma, true asthma, intrinsic asthma caused by pathophysiological disturbances, extrinsic asthma caused by environmental factors, essential asthma of unknown or inapparent cause, non-atopic asthma, bronchitic asthma, emphysematous asthma, exercise-induced asthma, occupational asthma, infective asthma caused by bacterial, fungal, protozoal or viral infection, non-allergic asthma, incipient asthma, wheezy infant syndrome;

chronic or acute bronchoconstriction, chronic bronchitis, small airway obstruction and emphysema;

obstructive or inflammatory airway disease of whatever type, etiology or pathogenesis, or an obstructive or inflammatory airway disease selected from the group consisting of asthma; pneumoconiosis, chronic eosinophilic pneumonia; chronic obstructive pulmonary disease (COPD),

COPD including chronic bronchitis, pulmonary emphysema or dyspnoea associated therewith, COPD that is characterised by irreversible, progressive airway obstruction, acute respiratory distress syndrome (ARDS), and exacerbation of airway hypersensitivity consequent to other medicament therapy;

pneumoconiosis of whatever type, etiology or pathogenesis, or pneumoconiosis selected from the group consisting of aluminosis, anthracosis (asthma), asbestosis, chalicosis, ptilosis caused by inhaling the dust from ostrich feathers, siderosis caused by the inhalation of iron particles, silicosis, byssinosis or cotton-dust pneumoconiosis and talc pneumoconiosis;

bronchitis of whatever type, etiology or pathogenesis, or bronchitis selected from the group consisting of acute bronchitis, acute laryngotracheal bronchitis, arachidic bronchitis, catarrhal bronchitis, croupus bronchitis, dry bronchitis, infectious asthmatic bronchitis, productive bronchitis, staphylococcal or streptococcal bronchitis; and vesicular bronchitis;

bronchiectasis of whatever type, etiology or pathogenesis, or bronchiectasis selected from the group consisting of cylindric bronchiectasis, sacculated bronchiectasis, fusiform bronchiectasis, capillary bronchiectasis, cystic bronchiectasis, dry bronchiectasis and follicular bronchiectasis;

seasonal allergic rhinitis, perennial allergic rhinitis, or sinusitis of whatever type, etiology or pathogenesis, or sinusitis selected from the group consisting of purulent or nonpurulent sinusitis, acute or chronic sinusitis, and ethmoid, frontal, maxillary, or sphenoid sinusitis;

rheumatoid arthritis of whatever type, etiology or pathogenesis, or rheumatoid arthritis selected from the group consisting of acute arthritis, acute gouty arthritis, primary chronic arthritis, osteoarthrosis, infectious arthritis, Lyme arthritis, progressive arthritis, psoriatic arthritis and spondylarthritis;

gout, and fever and pain associated with inflammation;

an eosinophil-related pathological disorder of whatever type, etiology or pathogenesis, or an eosinophil-related pathological disorder

selected from the group consisting of eosinophilia, pulmonary infiltration eosinophilia, Löffler's syndrome, chronic eosinophilic pneumonia, tropical pulmonary eosinophilia, bronchopneumonic aspergillosis, aspergilloma, eosinophilic granuloma, allergic granulomatous angijtis or Churg-Strauss syndrome, polyarteritis nodosa (PAN) and systemic necrotising vasculitis;

atopic dermatitis, allergic dermatitis, or allergic or atopic eczema;

urticaria of whatever type, etiology or pathogenesis, or urticaria selected from the group consisting of immune-mediated urticaria, complement-mediated urticaria, urticariogenic material-induced urticaria, physical stimulus-induced urticaria, stress-induced urticaria, idiopathic urticaria, acute urticaria, chronic urticaria, angiooedema, cholinergic urticaria, cold urticaria in the autosomal dominant form or in the acquired form, contact urticaria, giant urticaria and papular urticaria;

conjunctivitis of whatever type, etiology or pathogenesis, or conjunctivitis selected from the group consisting of actinic conjunctivitis, acute catarrhal conjunctivitis, acute contagious conjunctivitis, allergic conjunctivitis, atopic conjunctivitis, chronic catarrhal conjunctivitis, purulent conjunctivitis and vernal conjunctivitis;

uveitis of whatever type, etiology or pathogenesis, or uveitis selected from the group consisting of inflammation of all or part of the uvea, anterior uveitis, iritis, cyclitis, iridocyclitis, granulomatous uveitis, nongranulomatous uveitis, phacoantigenic uveitis, posterior uveitis, choroiditis and chorioretinitis;

psoriasis;

multiple sclerosis of whatever type, etiology or pathogenesis, or multiple sclerosis selected from the group consisting of primary progressive multiple sclerosis and relapsing remitting multiple sclerosis;

autoimmune/inflammatory diseases of whatever type, etiology or pathogenesis, or an autoimmune/inflammatory disease selected from the group consisting of autoimmune haematological disorders, haemolytic anaemia, aplastic anaemia, pure red cell anaemia, idiopathic thrombocytopenic purpura, systemic lupus erythematosus, polychondritis, scleroderma, Wegner's granulomatosis, dermatomyositis, chronic active hepati-

tis, myasthenia gravis, Stevens-Johnson syndrome, idiopathic sprue, autoimmune inflammatory bowel diseases, ulcerative colitis, Crohn's disease, endocrine ophthamopathy, Basedow's disease, sarcoidosis, alveolitis, chronic hypersensitivity pneumonitis, primary biliary cirrhosis, juvenile diabetes or type 1diabetes mellitus, anterior uveitis, granulomatous or posterior uveitis, keratoconjunctivitis sicca, epidemic keratoconjunctivitis, diffuse interstitial pulmonary fibrosis or interstitial pulmonary fibrosis, pulmonary cirrhosis, cystic fibrosis, psoriatic arthritis, glomerulonephritis with and without nephrotic syndrome, acute glomerulonephritis, idiopathic nephrotic syndrome, minimal change nephropathy, inflammatory/ hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, allergic contact dermatitis, benign familial pemphigus, pemphigus erythematosus, pemphigus foliaceus and pemphigus vulgaris;

prevention of foreign transplant rejection following organ transplantation;

inflammatory bowel disease (IBD) of whatever type, etiology or pathogenesis, or inflammatory bowel disease selected from the group consisting of ulcerative colitis (UC), collagenous colitis, colitis polyposa, transmural colitis and Crohn's disease (CD);

septic shock of whatever type, etiology or pathogenesis, or septic shock selected from the group consisting of renal failure, acute renal failure, cachexia, malarial cachexia, hypophysial cachexia, uremic cachexia, cardiac cachexia, cachexia suprarenalis or Addison's disease, cancerous cachexia, and cachexia as a consequence of infection by the human immunodeficiency virus (HIV);

liver damage;

pulmonary hypertension and hypoxia-induced pulmonary hypertension;

bone loss diseases, primary osteoporosis and secondary osteoporosis;

pathological disorders of the central nervous system of whatever type, etiology or pathogenesis, or a pathological disorder of the central nervous system selected from the group consisting of depression, Parkin-

son's disease, learning and memory disorders, tardive dyskinesia, drug dependence, arteriosclerotic dementia, and dementias that accompany Huntington's chorea, Wilson's disease, paralysis agitans and thalamic atrophies;

infections, especially viral infections, where these viruses increase the production of TNF-α in their host or where these viruses are sensitive to up-regulation of TNF-α in their host so that their replication or other vital activities are adversely affected, including viruses selected from the group consisting of HIV-1, HIV-2 and HIV-3, cytomegalovirus, CMV, influenza, adenoviruses and Herpes viruses, including Herpes zoster and Herpes simplex;

yeast and fungal infections, where these yeasts and fungi are sensitive to up-regulation by TNF-α or elicit TNF-α production in their host, for example fungal meningitis, particularly when administered in conjunction with other medicaments of choice for the treatment of systemic yeast and fungal infections, including, but not limited to, polymycins, for example polymycin B, imidazoles, for example clotrimazole, econazole, miconazole and ketoconazole, triazoles, for example fluconazole and itranazole, and amphotericins, for example amphotericin B and liposomal amphotericin B;

ischaemia-reperfusion damage, autoimmune diabetes, retinal autoimmunity, chronic lymphocytic leukaemia, HIV infections, lupus erythematosus, kidney and ureter diseases, pathological urogenital and gastrointestinal disorders and prostate diseases.

20. Use according to Claim 17, 18 or 19 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of (1) inflammatory diseases and conditions, including joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis and Crohn's disease; (2) airway diseases and conditions, including asthma, acute respiratory distress syndrome, chronic pulmonary

inflammatory disease, bronchitis, chronic obstructive airway disease and silicosis; (3) infectious diseases and conditions, including sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, fever and myalgia due to bacterial, viral or fungal infections, and influenza; (4) immune diseases and conditions, including autoimmune diabetes, systemic lupus erythematosus, GvH reaction, rejection of foreign transplants, multiple sclerosis, psoriasis and allergic rhinitis; and (5) other diseases and conditions, including bone absorption diseases, reperfusion damage, cachexia secondary to infection or malignancy, cachexia secondary to AIDS, human immunodeficiency virus (HIV) infection, or AIDS related complex (ARC), keloid formation, scar tissue formation, type 1 diabetes mellitus, and leukaemia.

21. Use according to Claim 17 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of myocardial diseases.

22. Use according to Claim 21 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of myocardial diseases, where these myocardial diseases have inflammatory and immunological properties.

23. Use according to Claim 17 of a compound of the formula I according to Claims 1 to 13 for the preparation of a medicament for the treatment of coronary heart disease, reversible or irreversible myocardial ischaemia/reperfusion damage, acute or chronic heart failure and restenosis, including in-stent restenosis and stent-in-stent restenosis.

24. Combination of a compound according to Claims 1 to 13 together with one or more members of the following group:

(a) leukotriene biosynthesis inhibitors: 5-lipoxygenase (5-LO) inhibitors and 5-lipoxygenase activating protein (FLAP) antagonists selected

from the group consisting of zileuton, ABT-761, fenleuton, tepoxalin, Abbott-79175, Abbott-85761, N-(5-substituted) thiophene-2-alkylsulfonamides, 2,6-di-tert-butylphenol hydrazones, Zeneca ZD-2138, SB-210661, the pyridinyl-substituted 2-cyanonaphthalene compound L-739,010, the 2-cyanoquinoline compound L-746,530, the indole and quinoline compounds MK-591, MK-886 and BAY x 1005;

(b) receptor antagonists for the leukotrienes LTB_4, LTC_4, LTD_4 and LTE_4 selected from the group consisting of the phenothiazin-3-one compound L-651,392, the amidino compound CGS-25019c, the benzoxazolamine compound ontazolast, the benzenecarboximideamide compound BIIL 284/260, the compounds zafirlukast, ablukast, montelukast, pranlukast, verlukast (MK-679), RG-12525, Ro-245913, iralukast (CGP 45715A) and BAY x 7195;

(c) PDE IV inhibitors;

(d) 5-lipoxygenase (5-LO) inhibitors; 5-lipoxygenase activating protein (FLAP) antagonists;

(e) dual inhibitors of 5-lipoxygenase (5-LO) and antagonists of platelet activating factor (PAF);

(f) leukotriene antagonists (LTRAs), including LTB_4 , LTC_4, LTD_4 and LTE_4 antagonists;

(g) antihistamine H_1 receptor antagonists, including cetirizine, loratadine, desloratadine, fexofenadine, astemizole, azelastine and chlorphenirамine;

(h) gastroprotective H_2 receptor antagonists;

(i) α_1- and α_2-adrenoreceptor agonist vasoconstrictor sympathomimetic agents administered orally or topically for decongestant use, selected from the group consisting of propylhexedrine, phenylephrine, phenylpropanolamine, pseudoephedrine, naphazoline hydrochloride, oxymetazoline hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride and ethylnorepinephrine hydrochloride;

(j) one or more α_1- and α_2-adrenoreceptor agonists as listed above under (i) in combination with one or more inhibitors of 5-lipoxygenase (5-LO) as listed above under (a);

(k) anticholinergic agents, including ipratropium bromide, tiotropium bromide, oxitropium bromide, pirenzepine and telenzepine;

(l) β_1- to β_4-adrenoreceptor agonists selected from the group consisting of metaproterenol, isoproterenol, isoprenaline, albuterol, salbutamol, formoterol, salmeterol, terbutaline, orciprenaline, bitolterol and pirbuterol;

(m) theophylline and aminophylline;

(n) sodium cromoglycate;

(o) muscarinic receptor (M1, M2 and M3) antagonists;

(p) COX-1 inhibitors (NSAIDs) and nitric oxide NSAIDs;

(q) the COX-2 selective inhibitor rofecoxib;

(r) insulin-like growth factor type I (IGF-1) mimetics;

(s) ciclesonide;

(t) inhalation glucocorticoids with reduced systemic side effects selected from the group consisting of prednisone, prednisolone, flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate and mometasone furoate;

(u) tryptase inhibitors;

(v) platelet activating factor (PAF) antagonists;

(w) monoclonal antibodies against endogenous inflammatory entities;

(x) IPL 576;

(y) antitumour necrosis factor (TNFα) agents selected from the group consisting of etanercept, infliximab and D2E7;

(z) DMARDs selected from the group consisting of leflunomide;

(aa) TCR peptides;

(bb) interleukin converting enzyme (ICE) inhibitors;

(cc) IMPDH inhibitors;

(dd) adhesion molecule inhibitors, including VLA-4 antagonists;

(ee) cathepsins;

(ff) MAP kinase inhibitors;

(gg) glucose 6-phosphate dehydrogenase inhibitors;

(hh) kinin B_1 and B_2 receptor antagonists;

(ii) gold in the form of an aurothio group together with various hydrophilic groups;

(jj) immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine and methotrexate;

(kk) anti-gout agents selected from the group consisting of colchicines;

(ll) xanthine oxidase inhibitors selected from the group consisting of allopurinol;

(mm) uricosuric agents selected from the group consisting of probenecide, sulfinpyrazone and benzbromarone;

(nn) antineoplastic agents, which are antimitotic medicaments selected from the group consisting of vinblastine and vincristine;

(oo) agents for promoting growth hormone secretion;

(pp) inhibitors of matrix metalloproteases (MMPs) selected from the group consisting of stromelysins, collagenases, gelatinases, aggrecanase, collagenase-1 (MMP-1), collagenase-2 (MMP-8), collagenase-3 (MMP-13), stromelysin-1 (MMP-3), stromelysin-2 (MMP-10) and stromelysin-3 (MMP-11);

(qq) transforming growth factor (TGFβ);

(rr) platelet-derived growth factor (PDGF);

(ss) fibroblast growth factor selected from the group consisting of basic fibroblast growth factor (bFGF);

(tt) granulocyte macrophage colony stimulating factor (GM-CSF);

(uu) capsaicin;

(vv) tachykinin NK_1 and NK_3 receptor antagonists selected from the group consisting of NKP-608C; SB233412 (talnetant) and D-4418;

(ww) elastase inhibitors selected from the group consisting of UT-77 and ZD-0892;

and

(xx) adenosine A_{2a} receptor agonists.

25. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 13 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

26. Set (kit) consisting of separate packs of

(a) an effective amount of a compound of the formula I according to one or more of Claims 1 to 13 and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and

(b) an effective amount of a further medicament active ingredient.